## B. In the Claims:

PLEASE ENTER THE FOLLOWING AMENDMENT WITHOUT PREJUDICE OR DISCLAIMER. Applicants reserve the right to file a divisional or continuation application to the originally filed claims.

## Claim 1 (Canceled)

- 2. (Previously Amended) The compound of claim 71, wherein the compound is isotopically enriched with three or more heavy atom isotopes.
- 3. (Previously Amended) The compound of claim 71, wherein the six-membered heterocyclic ring is substituted with one or more substituents.
- 4. (Original) The compound of claim 3, wherein the one or more substituents are alkyl, alkoxy or aryl groups.

#### Claims 5-7 (Canceled)

- 8. (Previously Amended) The compound of claim 71, wherein the six-membered heterocyclic ring comprises one or more additional nitrogen, oxygen or sulfur atoms.
- 9. (Previously Amended) The compound of claim 71, wherein LG is N-hydroxysuccinimide.
- 10. (Previously Amended) The compound of claim 71, wherein the compound is a salt.
- 11. (Previously Amended) The compound of claim 71, wherein the compound is a mono-TFA salt, a mono-HCl salt, a bis-TFA salt or a bis-HCl salt.

- 12. (Previously Amended) The compound of claim 71, wherein each incorporated heavy atom isotope is present in at least 80 percent isotopic purity.
- 13. (Previously Amended) The compound of claim 71, wherein each incorporated heavy atom isotope is present in at least 93 percent isotopic purity.
- 14. (Previously Amended) The compound of claim 71, wherein each incorporated heavy atom isotope is present in at least 96 percent isotopic purity.
- 15. (Previously Amended) An N-substituted morpholine acetic acid active ester compound of the formula:

or a salt thereof, wherein;

LG is the leaving group of an active ester selected from the group consisting of:

$$N-X'$$
 $N-X'$ 
 $N-X'$ 

X' is O or S;

each Z' is independently hydrogen, deuterium, fluorine, chlorine, bromine, iodine, an amino acid side chain or a straight chain or branched C1-C6 alkyl group that may optionally contain a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups each independently comprise linked hydrogen, deuterium or fluorine atoms; and

wherein the N-substituted morpholine acetic acid active ester is isotopically enriched with one or more heavy atom isotopes.

16. (Original) The compound of claim 15, wherein the N-substituted morpholine acetic acid active ester is isotopically enriched with three or more heavy atom isotopes.

### Claim 17 (Canceled)

- 18. (Original) The compound of claim 15, wherein LG is N-hydroxysuccinimide.
- 19. (Previously Amended) The compound of claim 15, wherein each Z' is independently hydrogen, deuterium, fluorine, chlorine, bromine or iodine.
- 20. (Currently Amended) The compound of claim 15, wherein each Z' is independently hydrogen, or methyl or methoxy.
- 21. (Previously Amended) The compound of claim 15, wherein X' is <sup>16</sup>O or <sup>18</sup>O.
- 22. (Original) The compound of claim 15, wherein the nitrogen atom of the morpholine ring is <sup>14</sup>N or <sup>15</sup>N.
- 23. (Previously Amended) The compound of claim 15, of the formula:

wherein;

each C\* is independently 12C or 13C;

LG is the leaving group of an active ester as defined in claim 15;

X' is O or S; and

each Z' is independently hydrogen, deuterium, fluorine, chlorine, bromine, iodine, an amino acid side chain or a straight chain or branched C1-C6 alkyl group that may optionally contain a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups each independently comprise linked hydrogen, deuterium or fluorine atoms.

- 24. (Original) The compound of claim 15, wherein the compound is a mono-TFA salt or a mono-HCl salt.
- 25. (Original) The compound of claim 15, wherein each incorporated heavy atom isotope is present in at least 80 percent isotopic purity.
- 26. (Original) The compound of claim 15, wherein each incorporated heavy atom isotope is present in at least 93 percent or isotopic purity.
- 27. (Original) The compound of claim 15, wherein each incorporated heavy atom isotope is present in at least 96 percent or isotopic purity.
- 28. (Previously Amended) An N-substituted piperidine acetic acid active ester compound of the formula:

or a salt thereof, wherein;

LG is the leaving group of an active ester selected from the group consisting of:

$$N-X'$$
 $N-X'$ 
 $N-X'$ 
 $N-X'$ 
 $NO_2$ 
 $NO_2$ 

X' is O or S;

each Z' is independently hydrogen, deuterium, fluorine, chlorine, bromine, iodine, an amino acid side chain or a straight chain or branched C1-C6 alkyl group that may optionally contain a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups each independently comprise linked hydrogen, deuterium or fluorine atoms; and

wherein the N-substituted piperidine acetic acid active ester is isotopically enriched with one or more heavy atom isotopes.

29. (Original) The compound of claim 28, wherein the N-substituted piperidine acetic acid active ester is isotopically enriched with three or more heavy atom isotopes.

## Claim 30 (Canceled)

- 31. (Original) The compound of claim 28, wherein LG is N-hydroxysuccinimide.
- 32. (Previously Amended) The compound of claim 28, wherein each Z' is independently hydrogen, deuterium, fluorine, chlorine, bromine or iodine.
- 33. (Currently Amended) The compound of claim 28, wherein each *Z'* is independently hydrogen, or methyl or methoxy.
- 34. (Previously Amended) The compound of claim 28, wherein X' is  $^{16}O$  or  $^{18}O$ .
- 35. (Original) The compound of claim 28, wherein the nitrogen atom of the piperidine ring is  $^{14}$ N or  $^{15}$ N.
- 36. (Previously Amended) The compound of claim 28, of the formula:

#### wherein;

each C\* is independently <sup>12</sup>C or <sup>13</sup>C;

LG is the leaving group of an active ester as defined in claim 28;

X' is O or S; and

each Z' is independently hydrogen, deuterium, fluorine, chlorine, bromine, iodine, an amino acid side chain or a straight chain or branched C1-C6 alkyl group that may optionally contain a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups each independently comprise linked hydrogen, deuterium or fluorine atoms.

- 37. (Original) The compound of claim 28, wherein the compound is a mono-TFA salt or a mono-HCl salt.
- 38. (Original) The compound of claim 28, wherein each incorporated heavy atom isotope is present in at least 80 percent isotopic purity.
- 39. (Original) The compound of claim 28, wherein each incorporated heavy atom isotope is present in at least 93 percent or isotopic purity.
- 40. (Original) The compound of claim 28, wherein each incorporated heavy atom isotope is present in at least 96 percent or isotopic purity.
- 41. (Previously Amended) An N-substituted piperazine acetic acid active ester compound of the formula:

or a salt thereof, wherein;

LG is the leaving group of an active ester selected from the group consisting of:

$$N-X'$$
 $N-X'$ 
 $N-X'$ 

X' is O or S;

Pg is an amine-protecting group;

each Z' is independently hydrogen, deuterium, fluorine, chlorine, bromine, iodine, an amino acid side chain or a straight chain or branched C1-C6 alkyl group that may optionally contain a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups each independently comprise linked hydrogen, deuterium or fluorine atoms; and

wherein the N-substituted piperazine acetic acid active ester is isotopically enriched with one or more heavy atom isotopes.

42. (Previously Amended) The compound of claim 41, wherein the N-substituted piperazine acetic acid active ester is isotopically enriched with three or more heavy atom isotopes.

### Claim 43 (Canceled)

- 44. (Original) The compound of claim 41, wherein LG is N-hydroxysuccinimide.
- 45. (Previously Amended) The compound of claim 41, wherein each Z' is independently hydrogen, deuterium, fluorine, chlorine, bromine or iodine.

- 46. (Currently Amended) The compound of claim 41, wherein each Z' is independently hydrogen, or methyl or methoxy.
- 47. (Previously Amended) The compound of claim 41, wherein X' is <sup>16</sup>O or <sup>18</sup>O.
- 48. (Original) The compound of claim 41, wherein each nitrogen atom of the piperazine ring is <sup>14</sup>N or <sup>15</sup>N.
- 49. (Previously Amended) The compound of claim 41, of the formula:

wherein,

each C\* is independently 12C or 13C;

LG is the leaving group of an active ester as defined in claim 41;

X' is O or S;

Pg is an amine protecting group; and

each Z' is independently hydrogen, deuterium, fluorine, chlorine, bromine, iodine, an amino acid side chain or a straight chain or branched C1-C6 alkyl group that may optionally contain a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups each independently comprise linked hydrogen, deuterium or fluorine atoms.

- 50. (Previously Amended) The compound of claim 41, wherein the compound is a mono-TFA salt, a mono-HCl salt, a bis-TFA salt or a bis-HCl salt.
- 51. (Original) The compound of claim 41, wherein each incorporated heavy atom isotope is present in at least 80 percent isotopic purity.

- 52. (Original) The compound of claim 41, wherein each incorporated heavy atom isotope is present in at least 93 percent or isotopic purity.
- 53. (Original) The compound of claim 41, wherein each incorporated heavy atom isotope is present in at least 96 percent or isotopic purity.

Claims 54-70 (Canceled)

71. (Currently Amended) A compound of formula:

or a salt thereof, wherein,

each carbon of the heterocyclic ring has the formula C(J)<sub>2</sub>;

W is an atom or group that is located ortho, meta or para to the ring nitrogen and is NH, N-R<sup>1</sup>, N-R<sup>2</sup>, P-R<sup>1</sup>, P-R<sup>2</sup>, O, C or S;

each J is the same or different and is H, deuterium (D),  $R^1$ ,  $OR^1$ ,  $SR^1$ ,  $NHR^1$ ,  $N(R^1)_2$ , fluorine, chlorine, bromine or iodine;

Z is O, S, NH or NR<sup>1</sup>; and

LG is an alcohol or thiol leaving group selected from the group consisting of:

$$N-X'$$
 $N-X'$ 
 $N-X'$ 

wherein,

X' is O or S;

R<sup>1</sup> is the same or different and is an alkyl group comprising one to eight carbon atoms which may optionally contain a heteroatom or a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups independently comprise linked hydrogen, deuterium and/or fluorine atoms; and

R<sup>2</sup> is an amino alkyl, hydroxy alkyl, thio alkyl group or a cleavable linker that cleavably links the reagent to a solid support wherein the amino alkyl, hydroxy alkyl or thio alkyl group comprises one to eight carbon atoms, which may optionally contain a heteroatom or a substituted or unsubstituted aryl group, and wherein the carbon atoms of the alkyl and aryl groups independently comprise linked hydrogen, deuterium and/or fluorine atoms; and

wherein the compound is isotopically enriched with one or more heavy atom isotopes.

# 72. (Previously Presented, Withdrawn) A method comprising:

- a) reacting an analyte with the compound of claim 71 to thereby produce a labeled analyte; and
- b) mixing the labeled analyte with one or more differentially labeled analytes.

73. (New) The compound of claim 71 of the formula:

74. (New) The compound of claim 71 of the formula: